

Fig. 1

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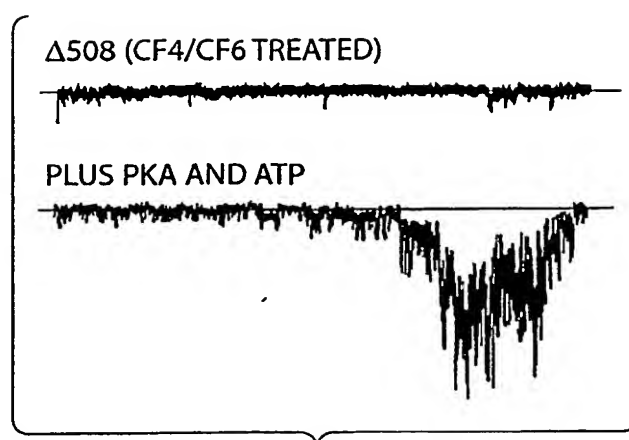


Fig. 2A

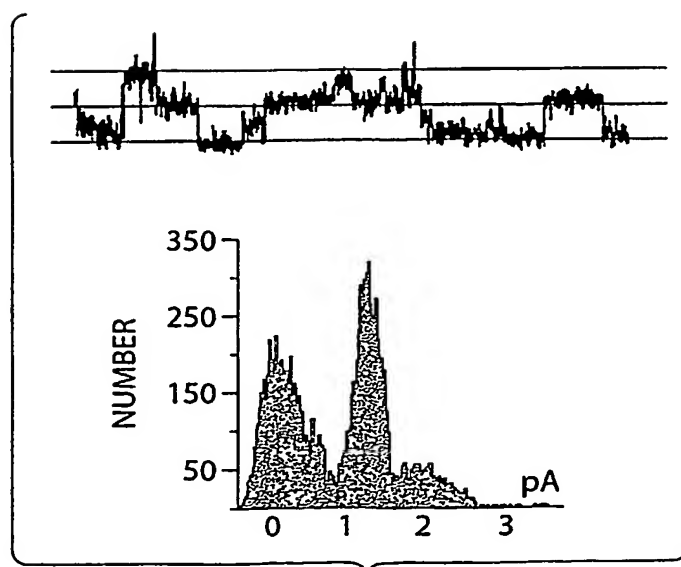


Fig. 2B

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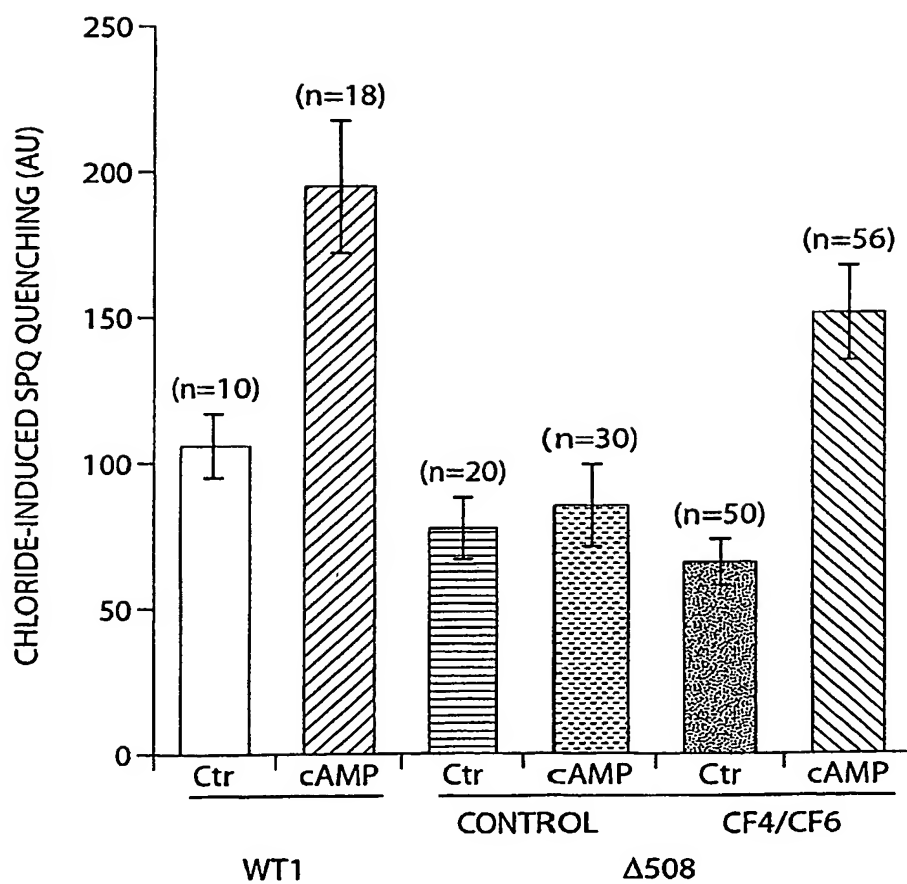


Fig. 3

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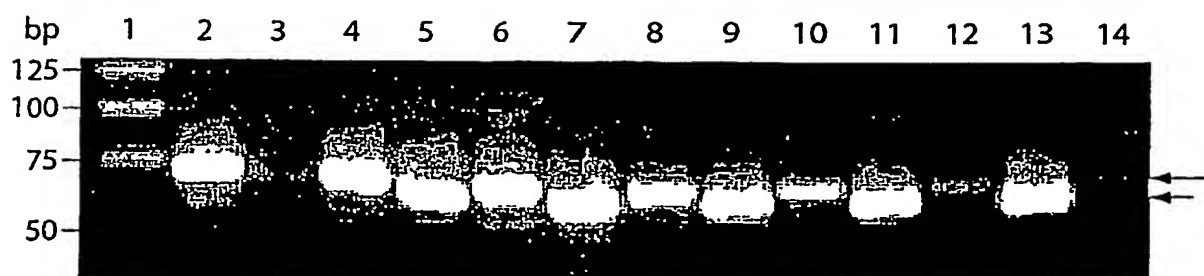


Fig. 4

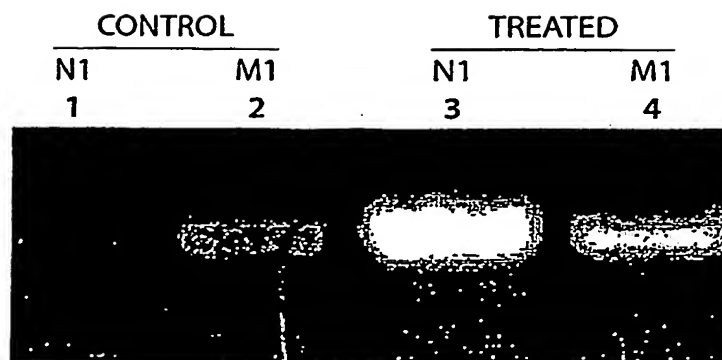


Fig. 5

BEST AVAILABLE COPY

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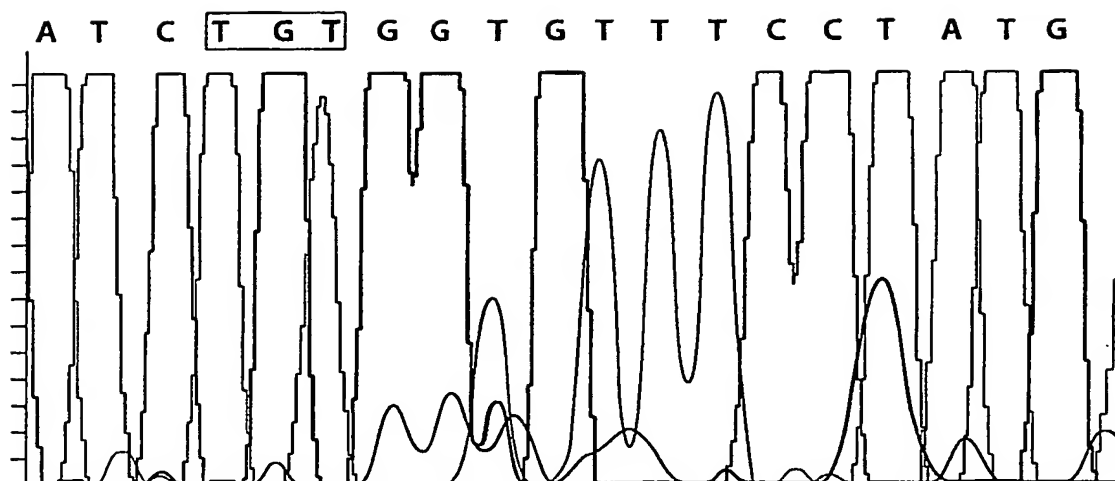
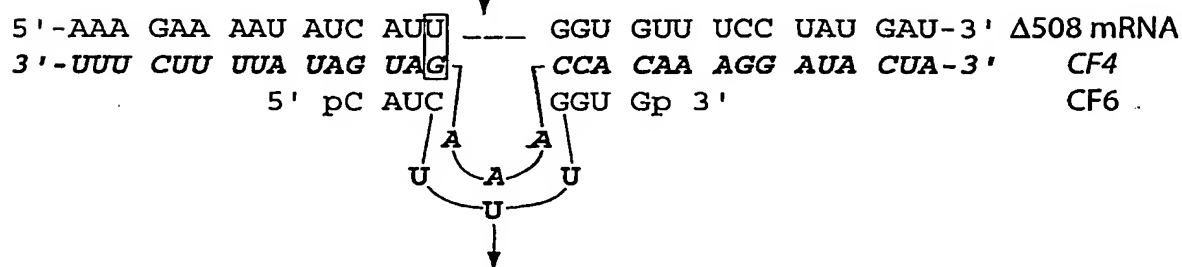


Fig. 6

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Δ508 mRNA REPAIR:

5' -AAA GAA AAU AUC AUC UUU GGU GUU UCC UAU GAU-3' WILD TYPE
 5' -AAA GAA AAU AUC AUU ---- GGU GUU UCC UAU GAU-3' Δ508 mRNA

TRIRIBONUCLEOTIDE Δ508 GENETIC DELETION**SCHEME 1****Fig. 7A****VARIED RIBONUCLEOTIDE INSERTION AND DELETION STEPS, WITH (c) BEING THE BEST RESULT:****REPEATED SEQUENCE ANALYSIS OF RT-PCR PRODUCTS WITH DIFFERENT PRIMERS:****(a) ARMS REVERSE PRIMER (N1)**

5' -AAA GAA AAU AUC A ---- UGU GGU GUU UCC UAU GAU-3'

(b) ARMS FORWARD PRIMER (NF1)

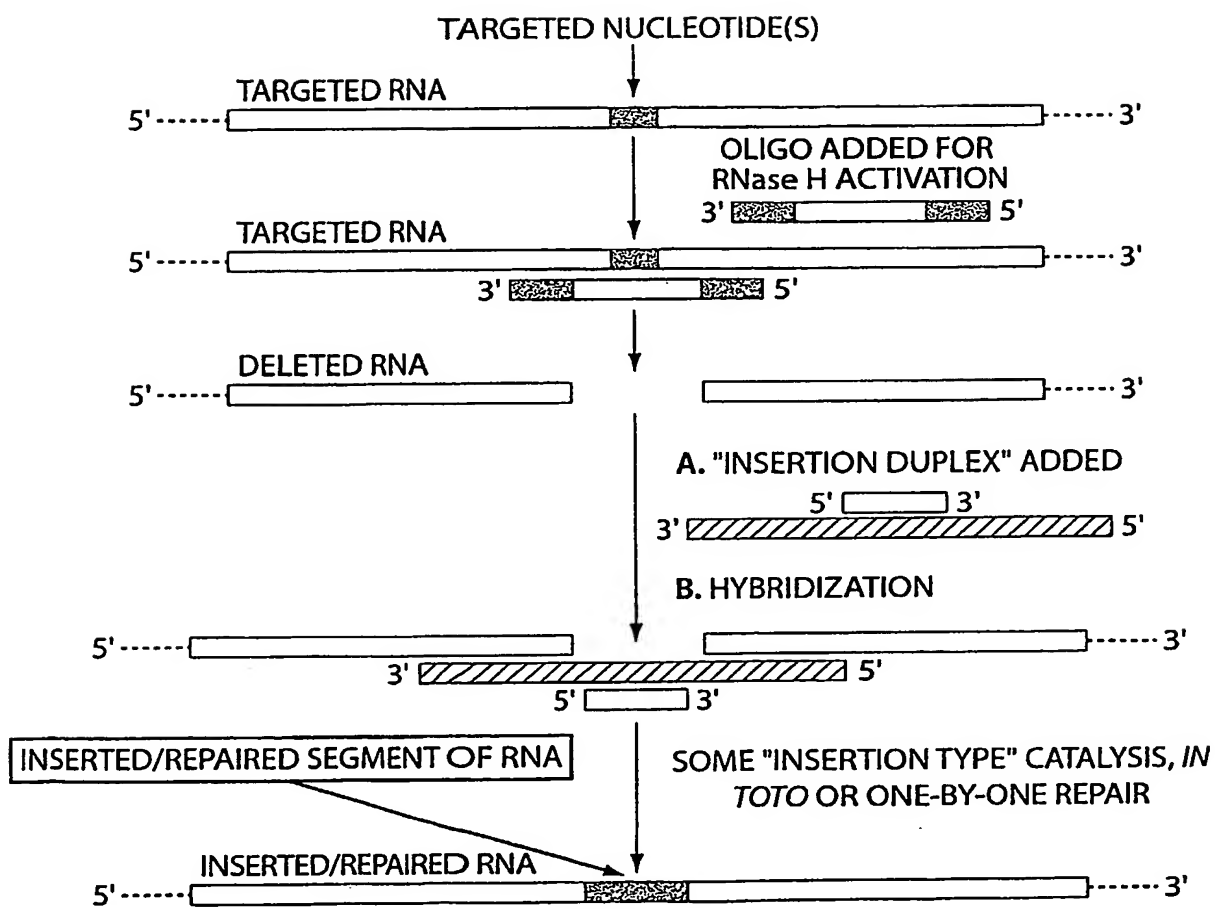
5' -AAA GAA AAU AUC AUC UGU ---- GUU UCC UAU GAU-3'

(c) ARMS FORWARD PS PRIMER (SNF1)

5' -AAA GAA AAU AUC AUC UGU GGU GUU UCC UAU GAU-3'

SCHEME 1**Fig. 7B**

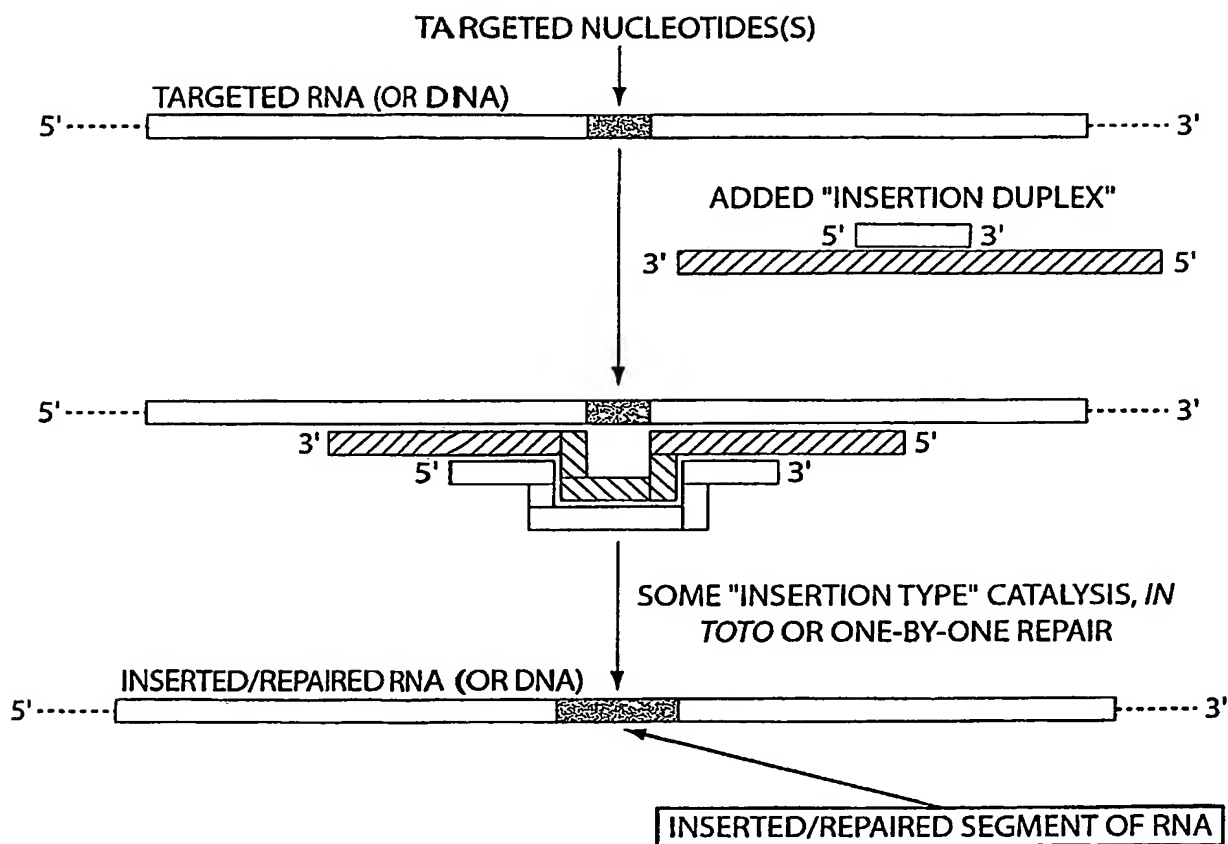
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SCHEME 2

Fig. 8

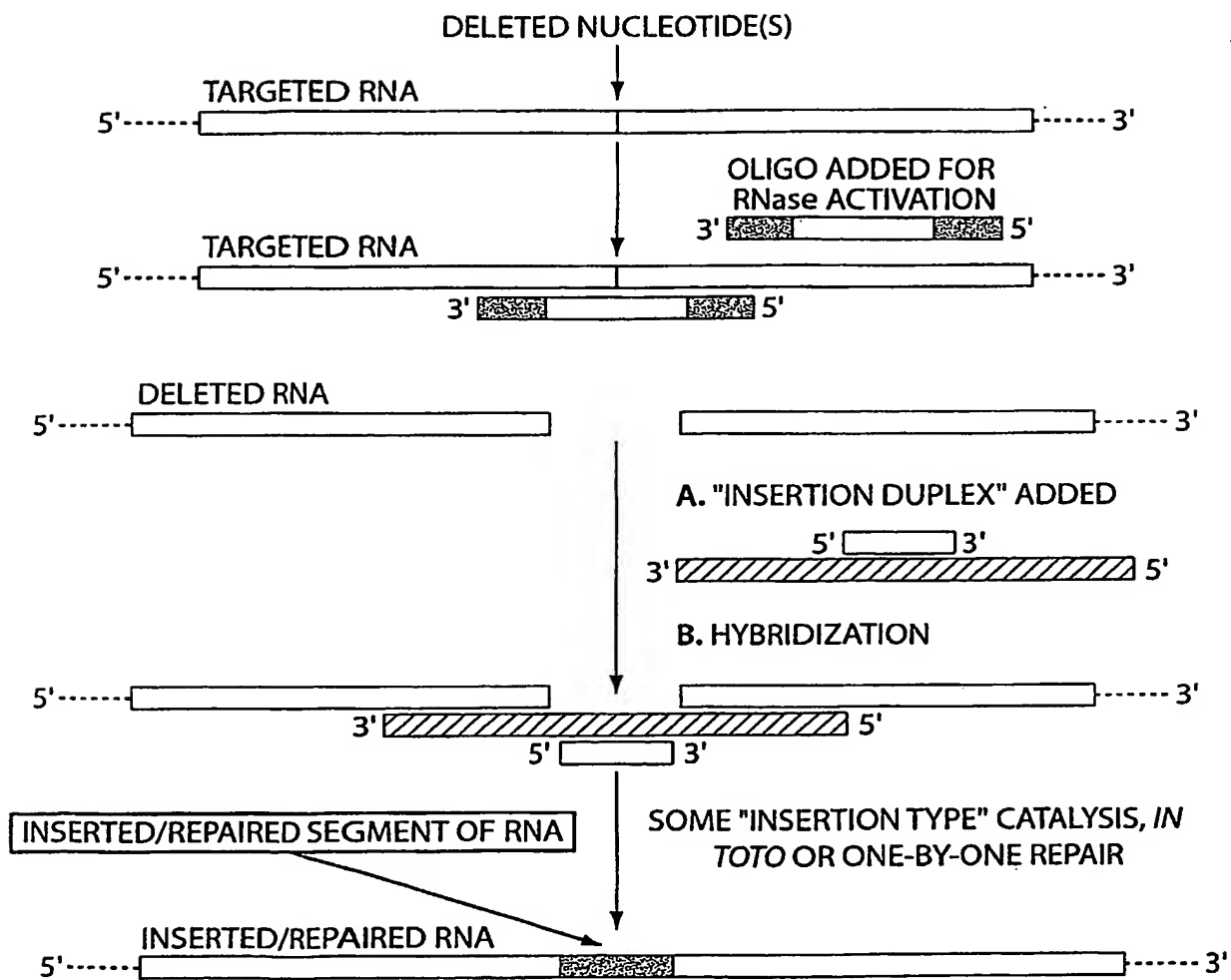
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SCHEME 3

Fig. 9

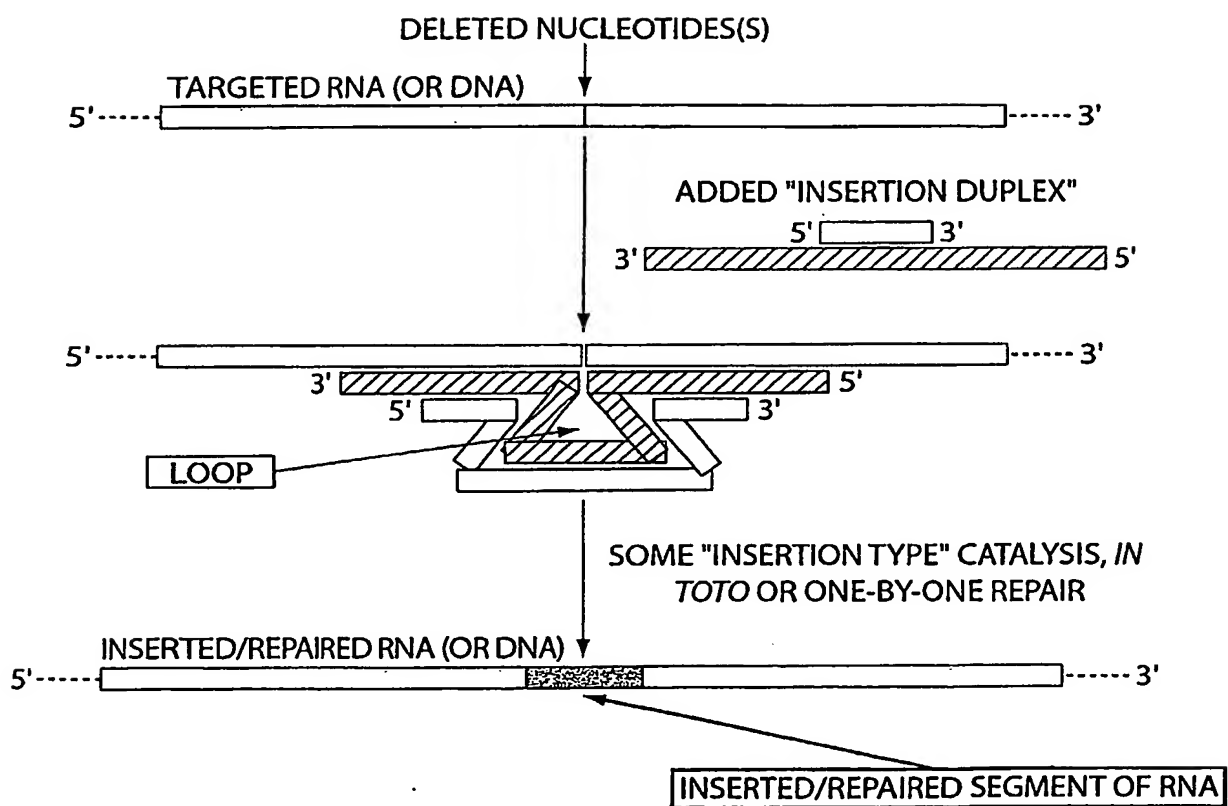
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SCHEME 4

Fig. 10

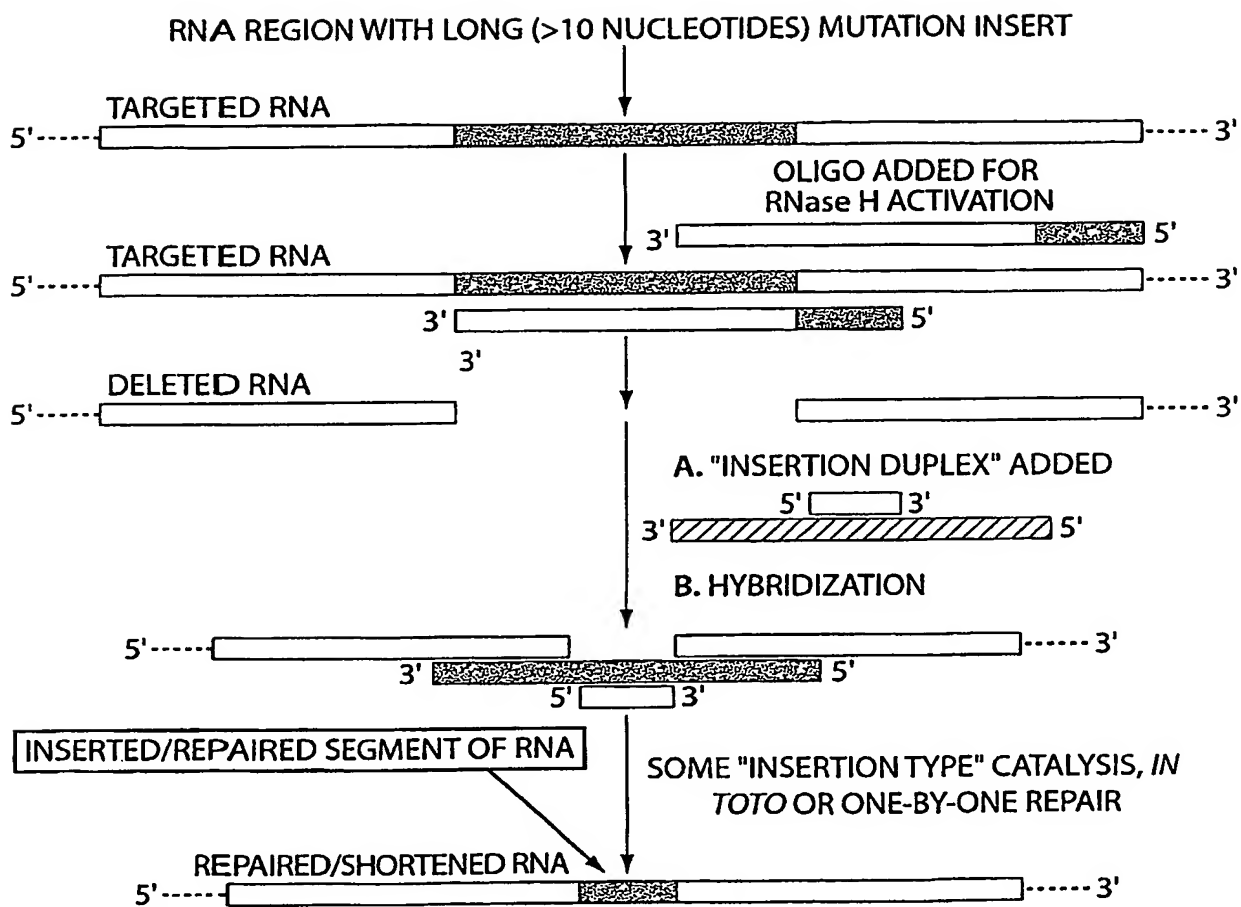
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SCHEME 5

Fig. 11

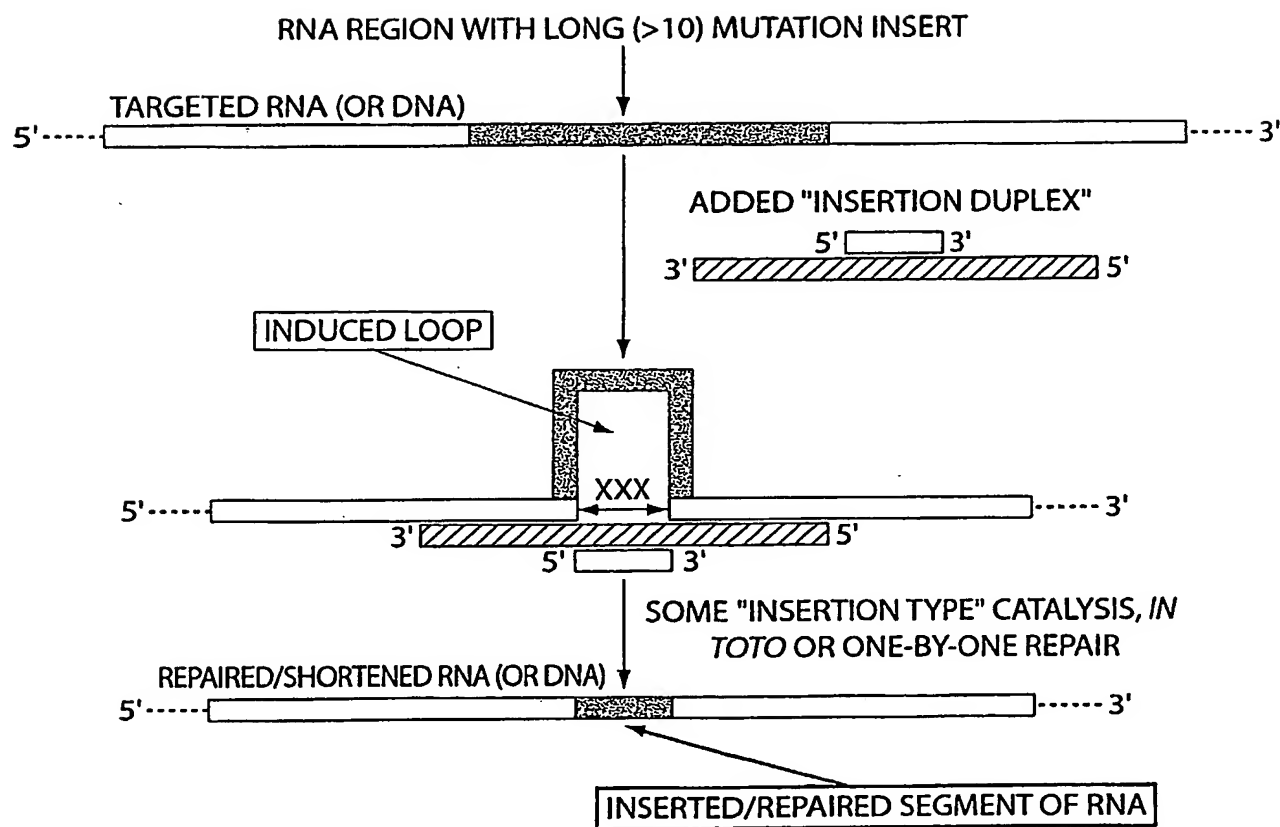
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SCHEME 6

Fig. 12

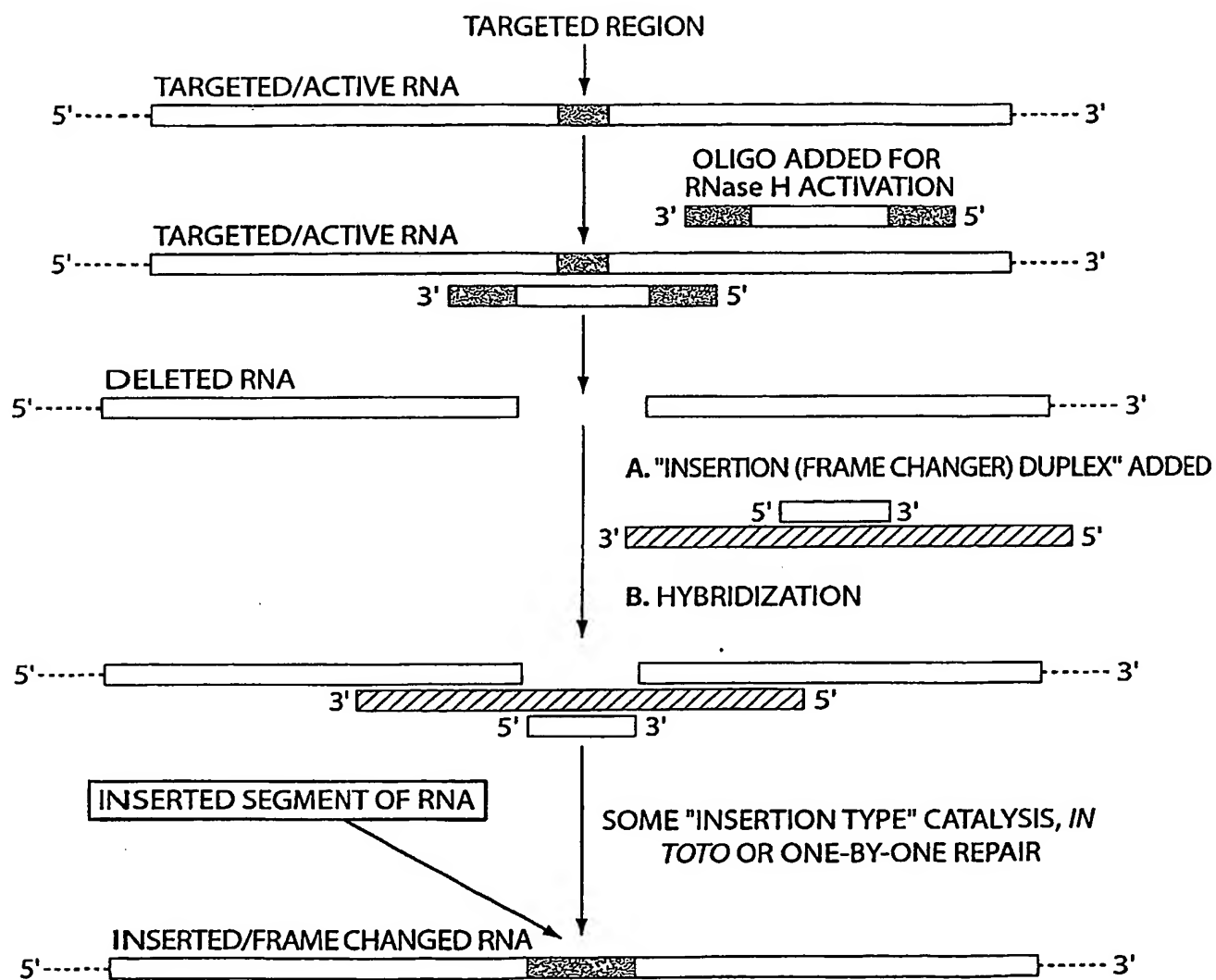
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SCHEME 7

Fig. 13

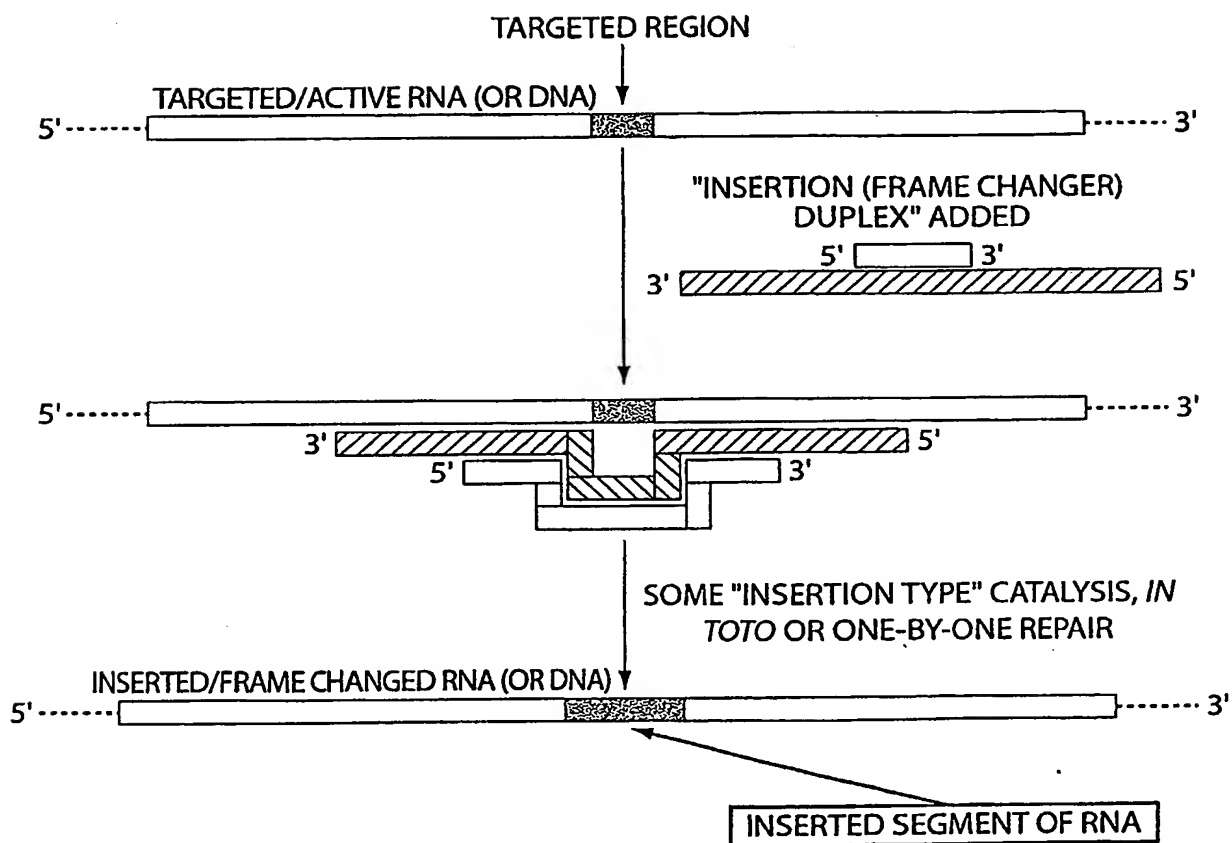
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SCHEME 8

Fig. 14

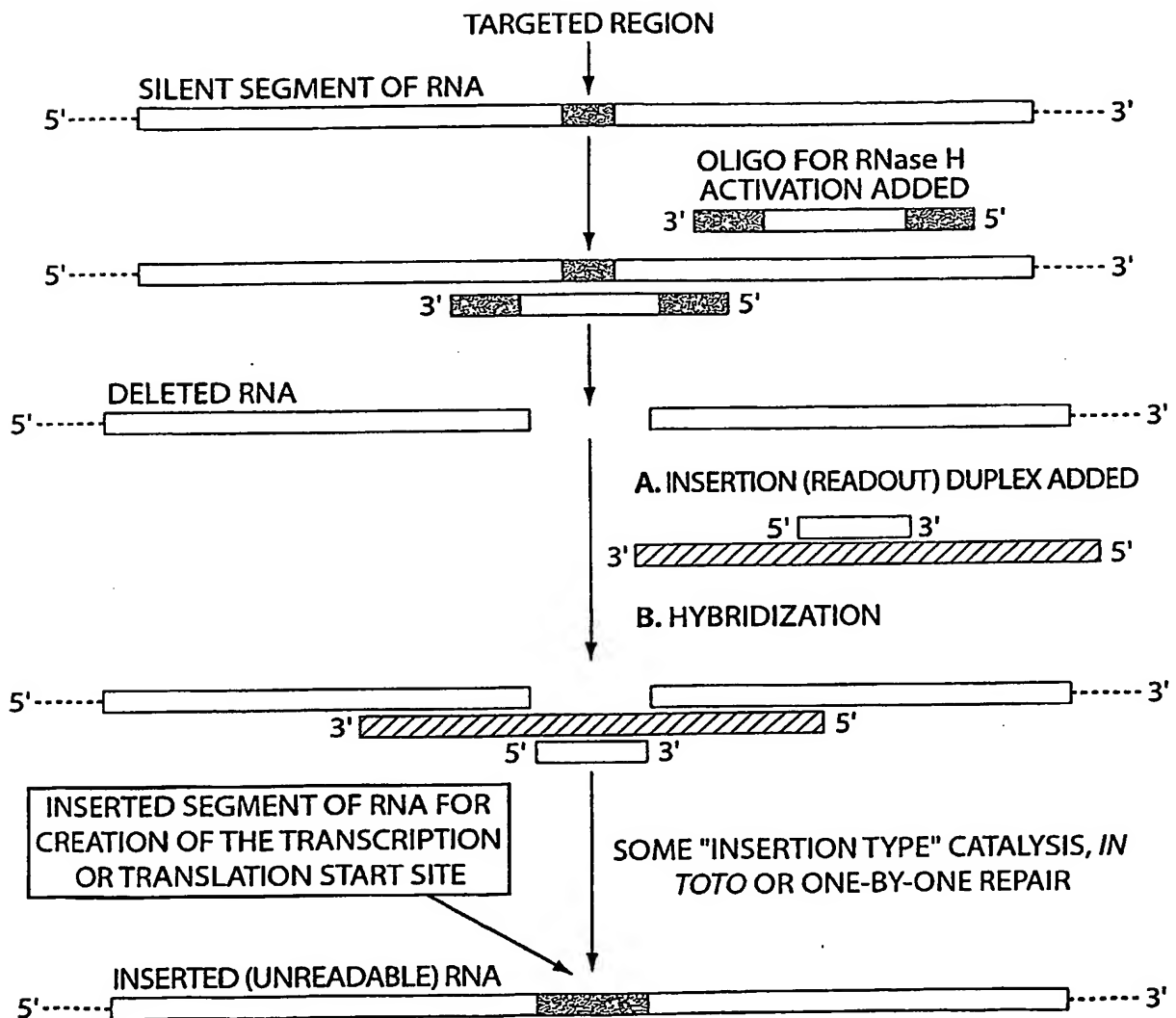
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SCHEME 9

Fig. 15

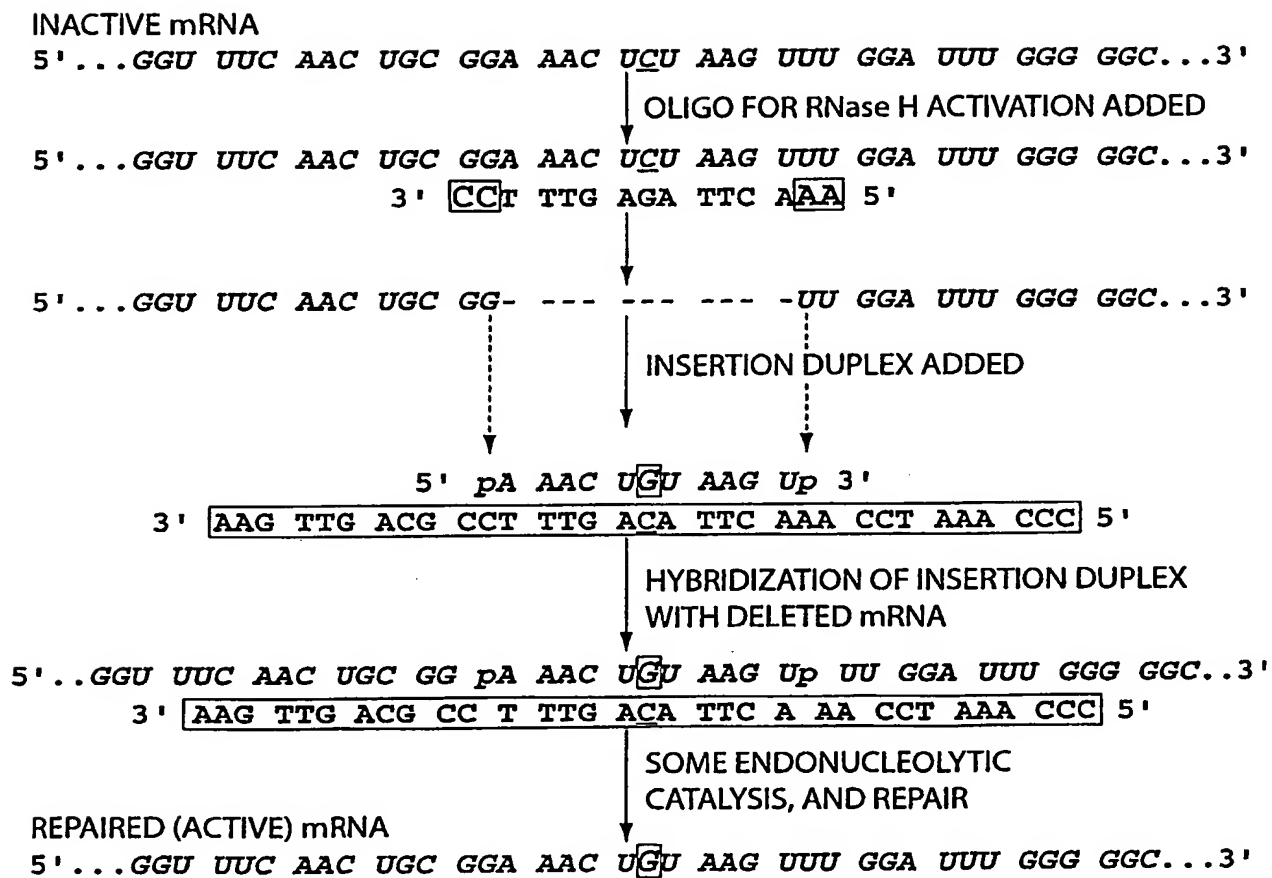
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SCHEME 10

Fig. 16

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SCHEME 11

Fig. 17

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INACTIVE mRNA

5'...GGU UUC AAC UGC GGA AAC UCU AAG UUU GGA UUU GGG GGC...3'

INSERTION DUPLEX ADDED

5'...GGU UUC AAC UGC GGA AAC U U AAG UUU GGA UUU GGG GGC...3'

3' AAG TTG ACG CCT TTG A A TTC AAA CCT AAA CCC 5'

5' pA AAC U UAAG Up 3'

SOME ENDONUCLEOLYTIC
CATALYSIS, AND REPAIR

REPAIRED (ACTIVE) mRNA

5'...GGU UUC AAC UGC GGA AAC UGU AAG UUU GGA UUU GGG GGC...3'

SCHEME 12

Fig. 18

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Δ508 mRNA REPAIR:

5'-AAA GAA AAU AUC AUC UUU GGU GUU UCC UAU GAU-3' WILD TYPE
 5'-AAA GAA AAU AUC AUU --- GGU GUU UCC UAU GAU-3' Δ508 mRNA

↑
 TRIRIBONUCLEOTIDE Δ508 GENETIC DELETION
 ↓

5'-AAA GAA AAU AUC AUU*GGU GUU UCC UAU GAU-3' Δ508 mRNA
 3' [A TAG] TAA CCA [CAA A] 5'

↓
 OLIGO FOR RNase H ACTIVATION ADDED
 ↓

5'--AAA GAA AAU AUC A---U GUU UCC UAU GAU-3'

↓
 PLUS INSERTION DUPLEX
 ↓

5'--AAA GAA AAU AUC A-----U GUU UCC UAU GAU-3'
 3' [UUU CUU UUA UAG UAG AAA CCA CAA AGG AUA CUA] 5'
 5' pC AUC UUU GGU Gp 3'

↓
 SOME ENDONUCLEOLYTIC CATALYSES, AND REPAIR
 ↓

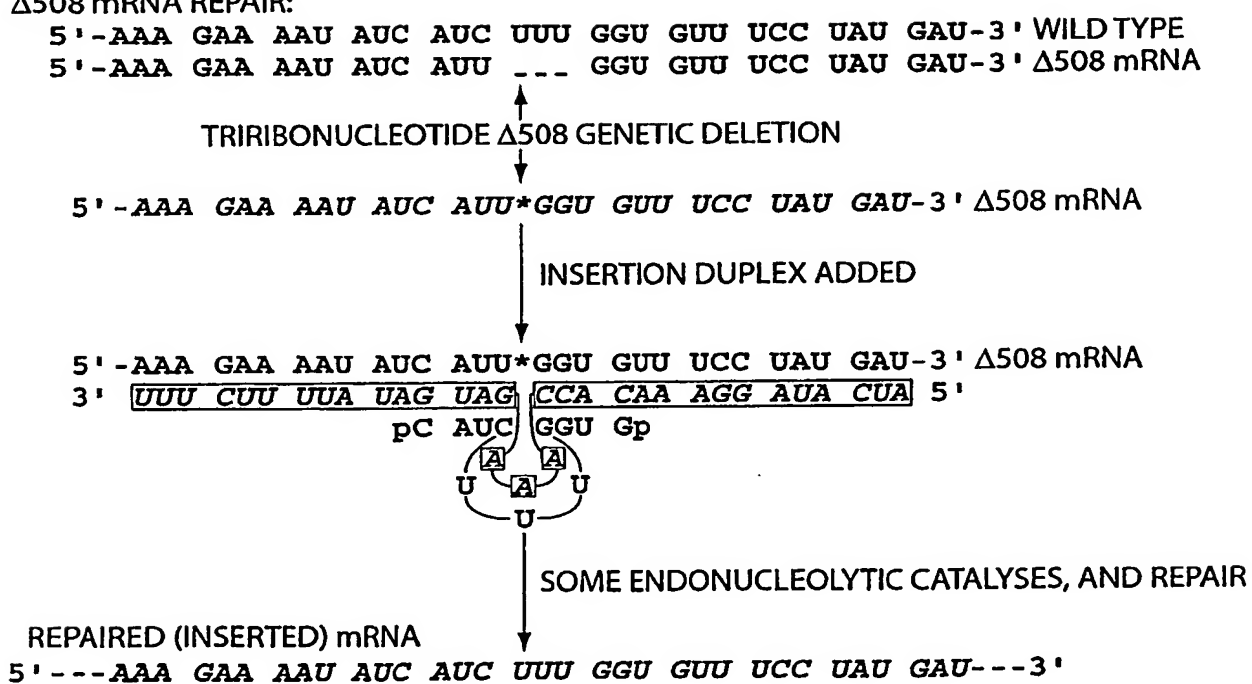
REPAIRED (INSERTED) mRNA

5'---AAA GAA AAU AUC AUC UUU GGU GUU UCC UAU GAU---3'

SCHEME 13

Fig. 19

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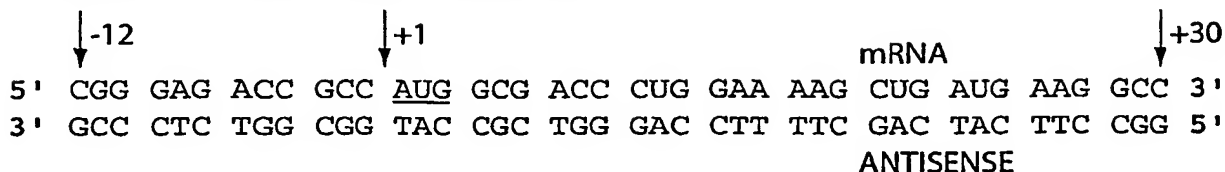
 Δ 508 mRNA REPAIR:

SCHEME 14

Fig. 20

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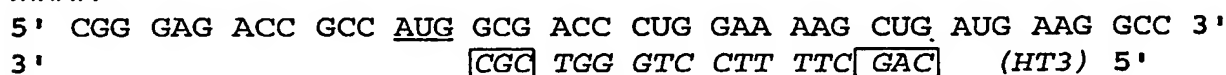
SEQUENCE OF mRNA FROM -12 POSITION



MECHANISM OF DELETION/INSERTION:

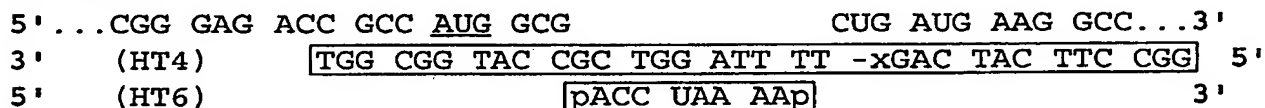
STEP 1 - ADDITION OF RNase H ACTIVATING OLIGONUCLEOTIDE (OLIGONUCLEOTIDE IDENTITY (ID) IS HT3)

mRNA



STEP 2 - ADDITION OF INSERTION DUPLEX (DUPLEX ID:HT4/HT6)

CUT mRNA



INSERTED mRNA



WILD TYPE mRNA (5'→3')

CGG GAG ACC GCC AUG GCG ACC CUG GAA AAG CUG AUG AAG GCC

MODIFIED mRNA



DELETED BASE

SCHEME 15

Fig. 21

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AIM-1 ALLELE OF MATP

MUTATED DUPLEX

5' AGC AGG ACC CTC AGG GCT-GTC AGC CAG TGG GAT GCA 3'
 3' TCG TCC TGG GAG TCC CGA-CAG TCG GTC ACC CTA CGT 5'

WILD TYPE

5' AGG ACC CTC AGG GCT CGT CGC T GTC AGC CAG TGC GAT GCA 3'
 3' TCC TGG GAG TCC CGA GCA GCG A CAG TCG GTC ACG CTA CGT 5'

MECHANISM OF DELETION/INSERTION:

MUTATED mRNA

5' AGC AGG ACC CUC AGG GCU GUC AGC CAG UGG GAU GCA 3'
 3' UCC CGA CAG UCG 5' (OLIGOS ID: Alb 3)

5' AGC AGG ACC CTC AGG-----AGC CAG TGG GAT GCA 3'
 3' UCC CGA CAG UCG 5' (OLIGOS ID: Alb 3)

Alb 4/Alb 6 DUPLEX ADDED

5' pGCU CGU CGC U GUCp 3' Alb6
 3' UGG GAG UCC CGA GCA GCG A CAG UCG GUC ACC 5' Alb4

REPAIRED mRNA

5' AGC AGG ACC CUC AGG GCU CGU CGC U GUC AGC CAG UGG GAU GCA

SCHEME 16

Fig. 22